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EXPERIMENTAL TYPHOID-PARATYPHOID CARRIERS

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The part played by the human carrier in the spread of typhoid fever is well known. The experience of various health departments shows that today flies, food (exclusive of milk), privies and sewage are relatively small factors in the dissemination of this disease. In the state of Massachusetts, according to O'Donnell,[1] few cases are due to water, especially in recent years, and in general no municipal supply is considered as a dangerous source of typhoid infection. Contact with true typhoid has been responsible for a few cases in homes and neighborhoods, while carriers have been proved to be responsible for 41.6% of cases of milkborne typhoid from 1915 to 1918, inclusive. It is therefore evident that carriers are a larger factor in the spread of typhoid than at present realized and are probably also the cause of an appreciable number of typhoid cases of unknown origin. This statement is supported by the fact that from 1915-1919, 14 carriers caused 249 cases of typhoid fever. Similar observations have been made by Chesley[2] and his associates, who traced 213 cases of typhoid fever in Minnesota to 30 carriers, or an average of 7 cases each. In California also the persistence of typhoid fever is definitely linked with carriers. Certain data collected in the army camps (Camp Dix) and in the Expeditionary forces clearly suggest that, in some instances, this mode of infection was responsible for small epidemics. Moreover, Garbat[3] has recently estimated that 55% of all typhoid may be traced directly or indirectly to carriers. The general reduction of typhoid in the United States has enabled the health authorities to devote more attention to the prevention of contact and carrier cases. A statement by Meader[4] summarizes the present situation in an excellent manner. He says: "By far the most difficult source of infection to trace and the most baffling to control is the typhoid carrier, and methods for the cure of typhoid carriers are among the most needy research problems."

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[1] Am. Jour. Public Health, 1920, 10, p. 517.

[2] Jour. Am. Med. Assn., 1917, 68, p. 1882.

[3] Ibid., 1916, 67, p. 1493.

[4] Mod. Med., 1920, 2, p. 244.

An elimination of typhoid fever can obviously only be expected when the problem dealing with the prevention and cure of carriers has been solved. Förster[5] has stated that if we can cure carriers we can get rid of typhoid fever. Unfortunately, it must be admitted that, hitherto, no certain method has been devised for rendering carriers typhoid-free. Biologic, as well as chemical, preparations have been applied to a limited number of intestinal carriers without any constant result. Surgical treatment, while not perfect, is at present considered the best available.

Since it is possible to produce in rabbits a condition similar to the carrier state in man, the new science of chemotherapy of bacterial infections has been tried extensively. The success so far achieved in rendering the rabbit carriers typhoid-free can be considered encouraging, but in no way striking. In all the experiments pertaining to the typhoid problem, it appears that therapeutic attempts have been made on a process, the pathogenesis of which is unknown, or in its best forn very superficially investigated. If the numerous tests had been crowned with success, which, as already stated has not been the case, one could attribute the result more to chance than to a well planned systematic investigation. Therapeutic studies must be preceded by an experimental analysis of the factors leading to a persistence of the typhoid bacilli in certain tissues, and with it to the carrier state. It is unquestionably true that the prevention of typhoid carriers can only be accomplished when the pathogenesis of this condition is known in detail.

These and similar considerations suggested in 1915 a systematic study of the typhoid infection in various laboratory animals. No attempt was made in using the words of Metchnikoff and Besredka,[6] "de resoudre le probléme de la fiévre typhoide si difficult et si compliqué." It was intended to place our knowledge concerning typhoid infection in rabbits on a broader basis. The subject was approached by making use of the well-known gall-bladder infections readily produced in these animals. It was soon realized that other laboratory animals must be included in the scope of the experimental observations. In dealing with so intricate a problem, on which a great deal had been written and which had been considered experimentally from so many different angles, the best working plan consisted in treating the typhoid bacillus and its allied organisms as living entities with an adaptive organization

[5] München. med. Wchnschr., 1908, 55, p. 1.
[6] Ann. de l'Inst. Pasteur., 1911, 25, p. 193.

and to follow them step by step in their passage through the animal body. The various phases of this investigation thus far completed with the aid of my collaborators will be summarized in a series of papers which will be submitted for publication as rapidly as other duties permit the undertaking.

The papers in preparation cover the following subjects: The Optimum H-ion Concentration for Growth of B. typhosus and B. paratyphosus A and B (paper 2); Do Carrier Strains differ from Strains Recently Isolated from Ordinary Typhoid Cases? (paper 3); A Comparative Study of the Infections Produced by Intravenous Injections of Typhoid, Paratyphoid A and B bacilli in Normal and Immunized Rabbits (paper 4); The Mechanism of Gallbladder Infection in Laboratory Animals (5); The Reaction and the Physiology of the Gallbladder and Hepatic Duct Bile of Laboratory Animals (6); The Bacteriostatic and Germicidal Properties of Bile (7); The Influence of the H-ion Concentration on the Growth of B. typhosus in Mediums Containing Bile or Bile Salts (8). Subsequent papers are planned to deal with: Feeding Experiments on Rabbits with B. typhosus and B. paratyphosus; Diet, Starvation and Immunization as Factors in the Production of the Intestinal Carrier State in the Rabbit; The Physical Properties of the Inoculum in the Production of Carriers; The Examination of Animal Stools as an Aid in the Diagnosis of the Carrier State; Renal Carriers in Rabbits; The Fate of B. typhosus and B. paratyphosus B Intravenously Inoculated into Guinea-Pigs, Cats, Rats and Monkeys; Typhoid and Paratyphoid A and B Infections Produced in Guinea-Pigs by Gallbladder Injections; Feedings of B. typhosus in Normal Guinea-Pigs and Those Suffering from "Deficiency" Disease; A Study of the Tissues Obtained from Experimental Carriers; and finally, A Correlation of the Experimental Results with the Facts Available from the Study of Human Carriers.